REMARKS

Claims 21 to 31 are currently pending in the subject application. Applicants have hereinabove canceled claims 22 and 26 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in the future. In addition, applicants have amended claims 21, 23, 25, 27, 30 and 31 to recite the term "antibody" which was recited in dependent claim 22 which has been cancelled hereinabove without prejudice. Support for the amendments to claim 21 can be found in the specification as originally filed at, *inter alia*, page 62, lines 16-18; page 57, lines 12-14; page 32, line 14 to page 33, line 2; and Fig. 15. Support for the term "antibody" in the amendments to claims 23, 25, 27, 30 and 31 can be found in the specification as originally filed at, *inter alia*, page 62, lines 16-18. Accordingly, applicants maintain that this Amendment raises no issue of new matter and respectfully request entry of this Amendment. After entry of this Amendment, claims 21, 23 to 25 and 27 to 31, as amended herein, will be pending and under examination.

Restriction Requirement

In the November 9, 2006 Office Action the Examiner stated that applicants are required to confirm that species antibody from group A and toxin from group B are being elected. In response, applicants hereby confirm the election of species antibody and toxin.

Declaration

The Examiner indicated that the Declaration is defective because the applications listed in the priority paragraph as amended should be listed in the Declaration.

In response, applicants will file a new Declaration, if necessary, once allowable subject matter is defined.

Claims rejected under 35 U.S.C. §112 (first paragraph)

The Examiner rejected claims 21, 23, 24 and 27-31 under 35 U.S.C. §112 as allegedly not enabled by the specification. The Examiner stated that the specification, while being enabling *for an antibody* for a prostate specific membrane antigen (PSM) does not reasonably provide enablement for other biological agents. The Examiner further stated, inter alia, that the specification does not disclose functional or structural attributes of the biological agent.

In response, applicants respectfully traverse the Examiner's rejection. Initially, applicants note that functional attributes of the biological agent are set forth in that the biological agent must, at the very least, bind to an outer membrane domain of prostate specific membrane antigen. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicants have herein amended independent claim 21, from which the other pending claims depend, directly or indirectly, to replace the term

"biological agent" with the term "antibody". Applicants note that the Examiner has stated that the specification is enabling for such an antibody. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims rejected under 35 U.S.C. §102(b)

Brinkmann et al.

The Examiner rejected claims 21, 22, 25 and 27-30 under 35 U.S.C. §102(b) as allegedly anticipated by Brinkmann et al. (PNAS, vol. 90, pages 547-551, March 1993).

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that claim 21 as amended recites that the antibody binds to an outer membrane domain of prostate-specific membrane antigen ("PSMA"). There is no indication, teaching or suggestion in Brinkmann et al. that monoclonal antibody PR1 binds to an outer membrane domain of PSMA. More particularly, Brinkmann et al. in the second paragraph of the Discussion on page 550 state that monoclonal antibody PR-1 binds to PC-3 cells and to about 1-3% of LNCaP cells. In contrast, applicants' specification teaches that, with regard to prostate-specific membrane antigen, there is a "uniformly *high* level of expression in LNCaP cells" and that PC-3 cells are *negative* for expression (emphasis added). See Figs. 17A-17C and Brief Description thereof at page 8, lines 31-37.

Applicants further note that the paper describing discovery of the monoclonal PR1 antibody, Ira Pastan et

al., (1993), J. Natl. Can. Inst. 85(14):1149-1154, attached hereto as **Exhibit 1**, notes that the antigen with which PR1 reacts is not present on prostate secretions. See page 1151, last paragraph. In contrast, prostate-specific membrane antigen is found on prostate secretions (see, Solokoff et al. (2000), *Prostate*, 43(2):150-57 and Troyer et al. (1995), *Int. J. Cancer* 62(5):552-558, attached hereto as **Exhibits 2 and 3** respectively).

Thus, applicants maintain that the PR1 antibody does not bind "to an outer membrane domain of prostate specific membrane antigen" as recited in claim 21. Accordingly, Brinkmann et al. do not teach the claimed invention, and applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Chu et al.

The Examiner rejected claims 21-25 and 27-31 under 35 U.S.C. §102(b) as allegedly anticipated by Chu et al. (U.S. Patent No. 4,939,240, issued July 1990) ("Chu et al."). The Examiner stated that Chu et al. disclose a method for treating cancer comprising a prostate carcinoma using monoclonal antibodies in conjunction with a pharmaceutical or cytotoxic agent (Col. 7, line 22-30 and col. 14, section 5.8.3 and table VIII). The Examiner further cited to the disclosure of the use of antibodies in Col. 44 of Chu et al.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that for raising the disclosed antibodies of Chu et al., "MCF-7 breast carcinoma cells were used as 'antigen'" (Col. 8, lines

59-61). However, applicants' specification clearly teaches that PSM (i.e. prostate-specific membrane antigen) is not expressed by MCF-7 breast carcinoma cells. See page 119, lines 9 to 13). Thus, the monoclonal antibodies of Chu et al. are not the monoclonal antibodies of applicants' claimed method. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Horoszewicz

The Examiner rejected claims under 35 U.S.C. §102(b)over Horoszewicz, U.S. Patent No. 5,162,504, issued November 1992 ("Horoszewicz"). The Examiner stated that Horoszewicz discloses a method of treating a prostate cancer with prostate antigen specific antibody conjugated with a toxin.

In response, applicants respectfully traverse the Examiner's rejection. Applicants note that the monoclonal antibody disclosed by Horoszewicz is that produced by the hybridoma 7E11-C5. However, the 7E11-C5 monoclonal antibody produced by this cell line binds to an intracellular epitope, i.e. "the intracellular domain at the very N-terminus of the PSMA molecule.." as stated in the abstract of Troyer et al. (1994), previously considered by the Examiner as item 36 of the Information Disclosure Statement filed March 26, 2004 in connection with the subject application. For the Examiner's convenience a copy of this Troyer et al. abstract is attached hereto as **Exhibit 4**. In addition, applicants note that the other monoclonal antibody disclosed in the '505 patent, namely 9H10-A4, "failed to react in frozen

sections with either normal prostatic epithelium or with neoplastic cells." See Col. 20, lines 13-16. Accordingly, applicants maintain that Horoszewicz does not disclose an "antibody which binds to an outer membrane domain of prostate specific membrane antigen" as recited in the claimed method. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.